

What is claimed is:

1. A pharmaceutical composition for transmucosal administration of a bioactive peptide or protein of interest comprising said bioactive peptide or protein of interest, a cationic polyamino acid, and a compatible buffer, wherein at the pH of the composition said compatible buffer does not cause precipitation of the cationic polyamino acid, and has a mono-anionic or neutral net charge; and  
5 wherein the transmucosal absorption of said bioactive peptide or protein is increased relative the absorption of said bioactive peptide or protein in the absence of said cationic polyamino acid.
2. The composition of claim 1, wherein the pH of said composition is between about pH 4.0 and about pH 6.0.
3. The composition of claim 1, wherein the pH of said composition is between about pH 4.0 and pH 5.0.
4. The composition of claim 1, wherein said compatible buffer is selected from the group consisting of acetic acid,  $\epsilon$ -aminocaproic acid or glutamic acid.
5. The composition of claim 1, wherein said compatible buffer comprises glutamic acid.
6. The composition of claim 1, further comprising a tonicifying agent, a viscosity-increasing agent, a bioadhesive agent, a preservative, or any combination thereof.
7. The composition of claim 1, wherein said cationic polyamino acid comprises poly-histidine, poly-arginine, poly-lysine, or any combination thereof.
8. The composition of claim 7, wherein said cationic polyamino acid has an average molecule weight of between about 10 kDa and about 200 kDa.

9. The composition of claim 1, wherein said bioactive peptide or protein is an exendin, an exendin analog, or an exendin derivative.
10. The composition of claim 1, wherein said bioactive peptide or protein is selected from the group consisting of exendin-3, exendin-4, exendin-4 acid, exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28), exendin-4 (1-28) amide, <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 amide, and <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 (1-28) amide.
11. The composition of claim 1, wherein said bioactive peptide or protein is selected from the group consisting of GLP-1, a GLP-1 analog, and a GLP-1 derivative.
12. The composition of claim 1, wherein said bioactive peptide or protein is selected from the group consisting of GLP-1, GLP-1 (7-37), GLP-1(7-36)NH<sub>2</sub>, Gly<sup>8</sup> GLP-1(7-37), Ser<sup>34</sup> GLP-1(7-37) Val<sup>8</sup> GLP-1(7-37) and Val<sup>8</sup> Glu<sup>22</sup> GLP-1(7-37).
13. The composition of claim 1, wherein said bioactive peptide or protein is selected from the group consisting of PYY peptides, PYY agonists and PYY derivatives.
14. The composition of claim 1, wherein said bioactive peptide is PYY or PYY (3-36).
15. The composition of claim 6, wherein said tonicifying agent is selected from the group consisting of sodium chloride, mannitol, sucrose, glucose and any combination thereof.
16. The composition of claim 6, wherein said viscosity-increasing agent is selected from the group consisting of: hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose of average molecular weight between about 10 and about 1,500 kDa, starch, gums and any combination thereof.
17. The composition of claim 6, wherein said bioadhesive agent is selected from the group consisting of: carbomer, polycarbophil and any combination thereof.

18. The composition of claim 6, wherein said preservative is selected from the group consisting of phenylethyl alcohol, methylparaben, ethylparaben, propylparaben, butylparaben, chlorbutanol, benzoic acid, sorbic acid, phenol, m-cresol, alcohol, and any combination thereof.

19. The composition of claim 1, wherein said absorption is increased at least 2 fold.

20. The composition of claim 1, wherein said absorption is increased at least 5 fold.

21. The composition of claim 1, wherein said absorption is increased at least 10 fold.

22. A pharmaceutical composition for transmucosal administration of a bioactive peptide or protein of interest comprising about 0.01% to about 5.0% (w/v) of said bioactive peptide or protein of interest; about 0.01% to about 1.0% (w/v) of a cationic polyamino acid having a molecular weight between about 10 kDa and about 200 kDa; and about 0.01% to about 10.0% (w/v) of a compatible buffer, wherein at of between about pH 4.0 and about 5.0, said compatible buffer does not cause precipitation of the cationic polyamino acid, and has a mono-anionic or neutral net charge; and wherein the transmucosal absorption of said bioactive peptide or protein is increased relative the absorption of said bioactive peptide or protein in the absence of said cationic polyamino acid.

23. The composition of claim 22, further comprising between about 0.001% to about 10.0% of a tonicifying agent.

24. The composition of claim 22, further comprising between about 0.001% to about 10.0% of a viscosity-increasing agent.

25. The composition of claim 22, further comprising between about 0.001% to about 10.0% of a bioadhesive agent.

26. The composition of claim 22, further comprising between about 0.001% to about 10.0% of a preservative.
27. A pharmaceutical composition for transmucosal administration comprising about 0.5% (w/v) of exendin-4; about 0.5% (w/v) of poly-arginine having an average molecular weight of about 141 kDa; and about 0.56% monosodium glutamate, monohydrate (w/v) at a pH of about 4.5.
28. The composition of claim 27, wherein said poly-arginine is poly-L-arginine.
29. The composition of claim 27, wherein said composition further comprises a tonicifying agent, a viscosity-increasing agent, a bioadhesive agent, a preservative, or any combination thereof.
30. The composition of claim 27, further comprising about 0.72% sodium chloride (w/v).
31. A pharmaceutical composition for transmucosal administration comprising about 0.5% (w/v) of exendin-4; about 1.0% (w/v) of poly-arginine having an average molecular weight of about 141 kDa; and about 0.56% monosodium glutamate, monohydrate (w/v) at a pH of about 4.5.
32. The composition of claim 31, wherein said poly-arginine is poly-L-arginine.
33. The composition of claims 31, wherein said composition further comprises a tonicifying agent, a viscosity-increasing agent, a bioadhesive agent, a preservative, or any combination thereof.
34. The composition of claim 31, further comprising about 0.72% sodium chloride (w/v).
35. A method for transmucosal administration of a bioactive peptide or protein comprising contacting a mucosal surface for a time sufficient for a therapeutically

effective amount of said bioactive peptide or protein to pass through the mucosal surface, with a composition comprising said bioactive peptide or protein of interest, a cationic polyamino acid, and a compatible buffer, wherein at the pH of the composition, said compatible buffer does not cause precipitation of the cationic polyamino acid, and has a mono-anionic or neutral net charge; and wherein the transmucosal absorption of said bioactive peptide or protein is increased relative the absorption of said bioactive peptide or protein in the absence of said cationic polyamino acid.

36. The method of claim 35, wherein said bioactive protein or peptide is an exendin, GLP-1 or an analog or derivative thereof and said dose is therapeutically effective in lower blood glucose.

37. The method of claim 36, wherein said exendin is selected from the group consisting of exendin-3, exendin-4, exendin-4 acid, exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28), exendin-4 (1-28) amide, <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 amide, and <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 (1-28) amide.

38. The method of claim 36, wherein said GLP-1 is selected from the group consisting of GLP-1, GLP-1 (7-37), GLP-1(7-36)NH<sub>2</sub>, Gly<sup>8</sup> GLP-1(7-37), Ser<sup>34</sup> GLP-1(7-37) Val<sup>8</sup> GLP-1(7-37) and Val<sup>8</sup> Glu<sup>22</sup> GLP-1(7-37).

39. The method of claim 35, wherein said bioactive protein or peptide is a PYY peptide or an analog or derivative thereof, and said dose is therapeutically effective in food intake, gastric emptying, pancreatic secretion or weight loss.

40. The method of claim 39, wherein said PYY peptide is PYY (3-36)

41. The method of claim 35, wherein said bioactive protein or peptide is an exendin, GLP-1 or an analog or derivative thereof and said dose is effective in causing weight loss.

42. The method of claim 41, wherein said exendin is selected from the group consisting of exendin-3, exendin-4, exendin-4 acid, exendin-4 (1-30), exendin-4 (1-

30) amide, exendin-4 (1-28), exendin-4 (1-28) amide, <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 amide, and <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 (1-28) amide.

43. The method of claim 41, wherein said GLP-1 is selected from the group consisting of GLP-1, GLP-1 (7-37), GLP-1 (7-36)NH<sub>2</sub>, Gly<sup>8</sup> GLP-1(7-37), Ser<sup>34</sup> GLP-1(7-37) Val<sup>8</sup> GLP-1(7-37) and Val<sup>8</sup> Glu<sup>22</sup> GLP-1(7-37).

44. A method for transmucosal administration of a bioactive peptide or protein comprising contacting a mucosal surface with a bioactive peptide or protein selected from the group consisting of exendin-3, exendin-4, exendin-4 acid, exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28), exendin-4 (1-28) amide, <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 amide, and <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 (1-28) amide for a time sufficient for a therapeutically effective amount of said bioactive peptide or protein to pass through the mucosal surface, with a composition comprising said bioactive peptide or protein of interest, poly-arginine having an average molecular weight of about 141 kDa; and glutamic acid at a pH of about 4.5; wherein the transmucosal absorption of said bioactive peptide or protein is increased relative the absorption of said bioactive peptide or protein in the absence of said poly-arginine.

45. A method for increasing the bioavailability of a bioactive peptide or protein of interest following transdermal administration comprising, combining said bioactive peptide or protein with a cationic polyamino acid and a compatible buffer, wherein at the pH of the composition, said compatible buffer does not cause precipitation of the cationic polyamino acid, and has a mono-anionic or neutral net charge; wherein the bioavailability of said bioactive peptide or protein is increased relative the bioavailability of said bioactive peptide or protein in the absence of said cationic polyamino acid.

46. The method of claim 45, wherein said bioactive protein or peptide is an exendin, GLP-1, a PYY peptide, or an analog or derivative of an exendin, GLP-1 or a PYY peptide.

47. The method of claim 46, wherein said exendin is selected from the group consisting of exendin-3, exendin-4, exendin-4 acid, exendin-4 (1-30), exendin-4 (1-

30) amide, exendin-4 (1-28), exendin-4 (1-28) amide, <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 amide, and <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 (1-28) amide.

48. The method of claim 46, wherein said GLP-1 is selected from the group consisting of GLP-1, GLP-1 (7-37), GLP-1(7-36)NH<sub>2</sub>, Gly<sup>8</sup> GLP-1(7-37), Ser<sup>34</sup> GLP-1(7-37) Val<sup>8</sup> GLP-1(7-37) and Val<sup>8</sup> Glu<sup>22</sup> GLP-1(7-37).

49. The method of claim 46, wherein said PYY peptide is PYY or PYY (3-36).

50. A method for increasing the bioavailability of a bioactive peptide or protein of interest following transdermal administration comprising, combining a bioactive peptide or protein selected from the group consisting of exendin-3, exendin-4, exendin-4 acid, exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28), exendin-4 (1-28) amide, <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 amide, and <sup>14</sup>Leu, <sup>25</sup>Phe exendin-4 (1-28) amide; with poly-arginine having an average molecular weight of about 141 kDa, and glutamic acid at a pH of about 4.5; wherein the bioavailability of said bioactive peptide or protein is increased relative the bioavailability of said bioactive peptide or protein in the absence of said poly-arginine.